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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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HARNESS, DICKEY & PIERCE, P.L.C. P.O. BOX 828 BLOOMFIELD HILLS, MI 48303			FORD, VANESSA L	
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			1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/725,188	Applicant(s) SIN ET AL.	
	Examiner Vanessa L. Ford	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12/5/2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-48 is/are pending in the application.
- 4a) Of the above claim(s) 23-26 and 37-44 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-22, 27-36 and 45-48 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 December 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
- Paper No(s)/Mail Date 8/23/05, 11/16/05.

- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 5, 2005 has been entered.

2. The text of those sections of the Title 35, U.S. code not included in this action can be found in the prior Office Action.

Rejections Withdrawn

3. In view of Applicant's amendment the following rejections are withdrawn.
- a) Rejection of claims 1, 27-29, 35-36 and 48 under 35 U. S.C. 102(a), pages 7-8, paragraph 6 of the Final Office action.
 - b) Rejection of claims 1-3, 5-6, 10-13, 15-16, 20-21, 27-35 and 48 under 35 U. S.C. 103(a), pages 12-14, paragraph 8 of the Final Office action.
 - c) Rejection of claims 1-3, 5-6, 10-13, 15-16, 20-22, 27-36 and 45-48 under 35 U. S.C. 103(a), pages 14-16, paragraph 9 of the Final Office action.
 - d) Rejection of claims 1-6, 10-16, 20-22, 27-36 and 45-48 under 35 U. S.C. 103(a), pages 14-16, paragraph 10 of the Final Office action.
 - e) Rejection of claims 1-22, 27-36 and 45-48 under 35 U. S.C. 103(a), pages 18-19, paragraph 11 of the Final Office action.

Rejections Maintained

4. The rejection under 35 U.S.C. 112, first paragraph is maintained for claims 1-22, 27-36 and 45-48 for the reasons set forth on pages 3-6, paragraph 5 of the Final Office Action.

The rejection was on the grounds that the claims are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the recombinant protein major adhesin protein of *Aeromonas hydrophila* (AHMA) does not reasonably provide enablement for derivatives of the recombinant protein major adhesin protein of *Aeromonas hydrophila*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification defines the term "polypeptide derivative" as any polypeptides in which one or more amino acids have been replaced by different amino acids and which retains the function or activity of the polypeptide (page 6). The specification fails to provide a structure for the, derivatives of the recombinant protein major adhesin protein of *Aeromonas hydrophila*.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Since the amino acid sequence of the protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity requires a knowledge with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expected intolerant to modification) and detailed knowledge of the ways in which the protein's structure relates to function. However, the problem of the prediction of protein's structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and outside of the realm of routine experimentation.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen multiple substitutions or multiple modifications of other types and the positions within the protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity are limited in any polynucleotide and the result of such modifications is unpredictable based on the instant disclosure. One skilled in the art would expect any tolerance to modifications, e.g., multiple substitutions. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acid modification in such protein.

Art Unit: 1645

Thomas E. Creighton, in his book, "*Proteins: Structures and Molecular Properties*, 1984", (page 315) teaches that variation of the primary structure of a protein can result in an instable molecule. He teaches that a single amino acid change can cause a mutant hemoglobin to have lower stabilities due to any of several causes: 1) alteration of close-packing of the interior; loss of one group that normally participates in a hydrogen bond or salt bridge; 2) the introduction of a charged or polar group into the interior or the insertion into a helical region of a proline residue, which must distort the alpha-helix; 3) while sometimes radical changes of surface groups, even introduction of a non-polar side chain- have no great effect on stability.

Thomas E. Creighton, in his book "*Protein Structure: A Practical Approach*, 1989; pages 184-186" teaches that present day site directed mutagenesis of a gene allows any amino acids in a protein sequence to be changed to any other, as well as introducing deletions and insertions". The reference goes on to teach that it is difficult to know which amino acid to change and which is the best residue to substitute for the desired functional and structural effect.

Nosoh, Y. et al in "*Protein Stability and Stabilization through Protein Engineering*, 1991" (chapter 7, page 197, second paragraph) adds support to Thomas E. Creighton, by teaching that results so far accumulated on the stability and stabilization of proteins appear to indicate that the strategy for stabilizing proteins differ from protein to protein and that any generalized mechanisms for protein stability have not yet been presented.

Factors to be considered in determining whether undue experimentation is required are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to selecting other proteins having claimed functional features, 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). One of skill in the art would require guidance, in order to make or use proteins that are derivatives of the recombinant protein major adhesin protein of *Aeromonas hydrophila* in a manner reasonable in correlation with the scope of the claims. Without proper guidance, the experimentation is undue.

The Applicant has not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of additions, deletions or substitutions. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made in the amino acid's structure and still maintain activity is unpredictable and the experimentation left those skilled in the art is unnecessarily and improperly, extensive and undue. See *Amgen Inc v Chugai*

Pharmaceutical Co Ltd. 927 F 2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and Exparte Forman, 230 U.S. P.Q. 546(Bd. Pat. App & int. 1986).

Applicant's Arguments

A) Applicant urges that the claims have been amended to recite that the AHMA protein is an isolated protein having the amino acid sequence of any one of SEQ ID NO: 2, 4 or 8 that the derivatives are conservative substituted versions thereof that are at least 75% homologous thereto and the derivatives and fragments are immunogenic.

B) Applicant urges that the sequences and homology limitation have been imported from copending US Patent Application No. 10/220,986 (Sin et al).

Applicant urges that description of conservative amino acid substitutions has also been imported into the present Specification from 10/220,986.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed December 5, 2005 have been fully considered but they are not persuasive.

The claims encompass any deletion or substitution including combinations thereof that are not defined. The instant specification has not taught which amino acids are deleted or substituted in the amino acid sequence to arrive at a derivative or fragment that is encompassed by the claimed invention. It should be remembered that the statute under 35 U.S.C. 112, first paragraph requires that Applicant teach how to make and use the claimed invention and not how to find fragments or derivatives of the

recombinant adhesin protein of *Aeromonas hydrophila*. One of skill in the art would not conclude that Applicant has enabled the polypeptides used in the claimed vaccine since the structure of the claimed polypeptides has not been disclosed. Therefore, Applicant has not meet the burden required under 35 U.S.C. 112, first paragraph. It should be noted that the enablement for the instantly claimed invention should not be based solely on the disclosure of a co-pending application (e.g. 10/220, 986). The instant specification does not provide enablement for the claimed invention. It should be remembered that each patent application is examined individually.

5. The rejection under 35 U.S.C. 102(b), Fang et al is maintained for claims 1-3, 5-6, 10 and 27-29 and 48 for the reasons set forth on page 11, paragraph 12 of the Final Office Action.

The rejection was on the grounds that Fang et al teach a vaccine composition comprising the 43 kDa major adhesin protein isolated from *Aeromonas hydrophila* and Freund's complete adjuvant (see the Abstract and page 139). Fang et al teach that the vaccine composition contained $150 \mu\text{g mL}^{-1}$ of the protein (page 139). The claim limitation "oral" is being viewed as a limitation of intended use. Claims limitations such as "wherein the proportion of water and oil in the emulsion further comprise 1:2, "wherein the proportion of water in the emulsion is equal" are being viewed as limitations of experimental design choice. Fang et al anticipate the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's vaccine with the vaccine of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the vaccine of the prior art does not possess the same material structural and functional characteristics of the claimed vaccine). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant's Arguments

- A) Applicant urges that in animals contact with Freund's complete adjuvant is reported as causing inflammation, induration, necrosis, hyperalgesia, chronic granulomasm ulcerations, abscesses, tissue sloughs, arthritis, neural or mechanical lameness and peritonitis. Applicant urges that ethical use of FCA is limited to non-oral use in those situations where no more humane substitute adjuvant is available.
- B) Applicant urges that Fang et al do not address whether or not a vaccine composition containing proteins that exhibit immunogenicity where parenterally placed directly into e.g. intramuscular, intravascular or intraperitoneal tissue can be administered orally to fish so to retain significant immunogenicity. Applicant urges that Fang et al do not teach AHMA proteins or their immunogenic fragments or derivatives in an orally administrable composition.

Examiner's response to Applicant's Arguments

Applicant's arguments filed December 5, 2005 have been fully considered but they are not persuasive.

- A) Fang et al teach a vaccine composition comprising *Aeromonas hydrophila*. To address Applicant's comments regarding the use of FCA, it should be noted that the claims are directed to a product, a vaccine, wherein at least one recombinant protein fragment and derivatives is emulsified in a water-in-oil emulsion (claim 2). Fang et al teach that the composition *Aeromonas hydrophila* is formulated in Freund's complete

adjuvant. It is the Examiner's position that Applicant is arguing limitations that are not in the claims with their comments regarding the ethical use of FCA.

B) It should be noted that the claim limitation "oral" is a limitation of intended use. It should be remembered that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963). Applicant has provided no side-by-side comparison to show that the claimed vaccine composition differs from that of the prior art. Therefore, this prior art reference anticipates the claimed invention.

New Grounds of Rejection

Provisional Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1 and 48 of this application are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 7, 9, 34, 35 and 36 of U.S. Patent application no. 10/220, 986. Although the conflicting claims are not identical, they are not patentably distinct from each other because both application are directed to vaccine compositions comprising the amino acid sequence as set forth in SEQ ID NOs. 2, 4 and 8. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1 and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite because the claims recite an improper Markush group. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being "selected from the group consisting of A, B and C." See *Ex parte Markush*, 1925 C.d. 126 (Comm'r Pat. 1925). It is unclear to which components are actually contained within the vaccine composition. Correction and or clarification is required.

8. Claims 1-22, 27-36 and 45-48 recite the term "immunologically sufficient amount". It is unclear as to what the applicant is referring? Clarification as to the meaning of this phrase is required.

9. Claim 48 recites the term "predetermined amount" predetermined volume". It is unclear as to what the applicant is referring? Clarification as to the meaning of this phrase is required.

It should be noted that the Examiner is interpreting the claims to be drawn to oral vaccines comprising an isolated recombinant adhesin protein of *Aeromonas hydrophila* (AHMA) selected from the group consisting of isolated recombinant adhesin proteins having the amino acid sequence as set forth in SEQ ID NO; 2, 4 or 8 or fragments thereof or derivatives thereof or variants having at least 75% homology to SEQ ID Nos. 2, 4 or 8 or immunogenic fragments thereof.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 1-6, 10, 27-29 35-36 and 48 are rejected under 35 U.S.C. 103(a) unpatentable over Fang et al (*Journal of Fish Diseases*, 2000, 23, 137-145) in view of Chen et al (*U.S. Patent No. 6,720, 001 B1*, published April 13, 2004).

Fang et al teach a vaccine composition comprising the 43 kDa major adhesin protein isolated from *Aeromonas hydrophila* and Freund's complete adjuvant (see the Abstract and page 139). Fang et al teach that the vaccine composition contained 150 $\mu\text{g mL}^{-1}$ of the protein (page 139).

Fang et al do not teach palm oil.

Chen et al teach the that organic oil such as palm oil can be used to provide improved delivery of polyfunctional active ingredients (columns 5 and 6). Chen et al teach that the present invention provides pharmaceutical oil-in-water emulsion for the deliver of polyfunctional active ingredients (see the Abstract). Chen et al teach that the compositions of the invention that contain organic oils such as palm oil are stable compositions (column 5). The claim limitation "oral" is being viewed as a limitation of intended use. Claims limitations such as "wherein the proportion of water and oil in the emulsion further comprise 1:2, "wherein the proportion of water in the emulsion is equal" are being viewed as limitations of experimental design choice. The claim limitation "...prepared by a method comprising the steps of..." is being viewed as a process limitation. The products of the prior art reference appear to be the same as the product claimed by the applicant because they appear to possess the same functional characteristics. The purification or production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art. This is particularly true when properties of the product are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPO 964 (CAFC 1985); In re Marosi, 218 USPO 289, 29222-293 (CAFC 1983); In re Brown, 173 USPO 685 (CCPA 1972). Even if applicant's product can be shown to be of higher purity than the product of the prior art reference, applicant's needs to show some unexpected and unique utility or property, such as unexpected biologically significant increase in specific activity with which the increased purity, greater stability and/or practicality or freedom from some restrictive element or adverse side effects inherent in the product

preparations of the prior art or some other secondary consideration which the additional degree of purity imparts (to which there is a basis in the specification) to applicant's product in order to overcome the aspect of the product's purity is relied upon.

It would be *prima facie* obvious at the time the invention was made to add the palm oil as taught by Chen et al to the vaccine composition of Fang et al a because Chen et al teach the that organic oil such as palm oil can be used to provide improved delivery of polyfunctional active ingredients (columns 5 and 6). It would be expected barring evidence to the contrary that a vaccine comprising palm oil would be effective stabilizing vaccines at improving delivery of polyfunctional active ingredients.

11. Claims 7-9 are rejected under 35 U.S.C. 103(a) unpatentable over Fang et al in view of Chen et al (*U.S. Patent No. 6,720, 001 B1, published April 13, 2004*) as applied to claims 1-6, 27-29, 35, 36 and 48 and further view of Calanchi et al (*U.S. Patent No. 5,008,117, published April 16, 1991*).

Claims 7-9 are drawn to the oral composition wherein the oral vaccine is mixed with a binding agent.

Calanchi et al teach binding agents such as carboxymethylcellulose (column 3). Calanchi et al teach that binders are soluble in water and solvents (column 3). Calanchi et al teach that binders are often used to thicken the composition (column 4).

It would be *prima facie* obvious at the time the invention was made to add carboxymethylcellulose as taught by Calanchi et al to the vaccine composition of Fang

et al and Chen et al as combined above because Calanchi et al teach that binders are often used to thicken the composition and have the property of dispersing and dissolving quickly in water or aqueous vehicles (see the Abstract). It would be expected barring evidence to the contrary that a vaccine comprising binding agents such as carboxymethylcellulose would be effective at making the components of the composition easily to disperse and dissolve quickly in water or aqueous vehicles.

12. Claims 1-3, 5-6, 10, 15-16, 20-21, 27-36, 45 and 48 are rejected under 35 U.S.C. 103(a) unpatentable over Wolf-Watz et al (*U.S. Patent No. 5,284,653 published February 8, 1994*) in view of Fang et al (*Journal of Fish Diseases, 2000, 23, 137-145*).

Claims 1-3, 5-6, 10, 15-16, 20-21, 27-36, 45 and 48 are drawn to an oral vaccine comprising at least one recombinant protein AHMA, recombinant protein AHMA fragments and recombinant protein derivatives further comprising recombinant protein FP.

Wolf-Watz et al teach a fish vaccine comprising multiple fish antigens (see the Title and the Abstract). Wolf-Watz et al teach that the invention contemplates that the mutant strain of the invention may carry DNA sequences coding for an antigenic determinants from other fish pathogens and is capable of expressing the sequence (column 6). Wolf-Watz et al teach that the invention contemplates vaccines comprising bacteria the carry multiple determinants from different pathogenic fish and capable of expressing hybrid (fusion) determinants (column 7). Wolf-Watz et al teach that viruses such as infectious pancreatic necrosis virus and infectious hematopoietic necrosis virus may apart of the vaccine of the invention (column 6). Wolf-Watz et al teach that the

bacteria of the invention contains 1×10^2 - 1×10^8 bacteria/ml (column 8). Wolf-Watz et al teach that the vaccine of the invention can be added to fish feed (column 8).

Wolf-Watz et al do not teach the 43 kDa major adhesin protein isolated from *Aeromonas hydrophila*.

Fang et al teach a vaccine composition comprising the 43 kDa major adhesin protein isolated from *Aeromonas hydrophila* and Freund's complete adjuvant (see the Abstract and page 139). Fang et al teach that the vaccine composition contained $150 \mu\text{g mL}^{-1}$ of the protein (page 139). The claim limitation "oral" is being viewed as a limitation of intended use. Claims limitations such as "wherein the proportion of water and oil in the emulsion further comprise 1:2, "wherein the proportion of water in the emulsion is equal" are being viewed as limitations of experimental design choice. The claim limitation "...prepared by a method comprising the steps of..." is being viewed as a process limitation. The products of the prior art reference appear to be the same as the product claimed by the applicant because they appear to possess the same functional characteristics. The purification or production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art. This is particularly true when properties of the product are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPO 964 (CAFC 1985); In re Marosi, 218 USPO 289, 29222-293 (CAFC 1983); In re Brown, 173 USPO 685 (CCPA 1972). Even if applicant's product can be shown to be of higher purity than the product of the prior art reference, applicant's needs to show some unexpected and unique utility or property, such as unexpected biologically significant

increase in specific activity with which the increased purity, greater stability and/or practicality or freedom from some restrictive element or adverse side effects inherent in the product preparations of the prior art or some other secondary consideration which the additional degree of purity imparts (to which there is a basis in the specification) to applicant's product in order to overcome the aspect of the product's purity is relied upon.

It would be *prima facie* obvious at the time the invention was made to add the isolated recombinant adhesin protein from *Aeromonas hydrophila* as taught by Fang et al to the vaccine composition of Wolf-Watz et al because Wolf-Watz et al teach that the vaccine of the invention may comprise one or more antigens that are pathogenic to fish to produce a vaccine that provides broad spectrum protection against a range of fish pathogens (column 7). It would be expected barring evidence to the contrary that a vaccine comprising proteins from *Aeromonas hydrophila* and the 43 kDa major adhesin protein isolated from *Aeromonas hydrophila* would be effective in protecting against a broad spectrum of fish diseases.

13. Claims 11-13 are rejected under 35 U.S.C. 103(a) unpatentable over Wolf-Watz et al, Fang et al as set forth above for claims 1-3, 5-6, 10, 15-16, 20-21, 27-36, 45 and 48 and further in view of Wang et al (*Fish Shellfish Immunol.*, Nov. 2002;13(5):337-50).

Claims 11-13 are drawn to the oral vaccine of claim 1 further comprising recombinant protein comprising immobilization antigen repeat I of *Ichthyophythrirus multifiliis*

Wolf-Watz et al and Fang et al do not teach the immobilization antigen repeat I of *Ichthyophytherius multifiliis* (FP).

Wang et al teach a vaccine composition comprising the immobilization antigen repeat I of *Ichthyophytherius* and Freund's incomplete adjuvant (see the Abstract). Wang et al teach that fish immunized with the FP antigen developed high titers of serum immobilized antibodies (see the Abstract). Wang et al teach that this study shows there is a clear role for the immobilization antigen repeat I of *Ichthyophytherius* in protection (see the Abstract). The claim limitation "recombinant" is being viewed as a process limitation.

It would be *prima facie* obvious at the time the invention was made to add the immobilization antigen repeat I of *Ichthyophytherius* as taught by Wang et al to the vaccine composition of Wolf-Watz et al and Fang as combined above because Wolf-Watz et al teach that the vaccine of the invention may comprise one or more antigens that are pathogenic to fish to produce a vaccine that provides broad spectrum protection against a range of fish pathogens (column 7). It would be expected barring evidence to the contrary that a vaccine comprising the isolated recombinant adhesin protein of *Aeromonas hydrophila* and immobilization antigen repeat I of *Ichthyophytherius* would be effective in protecting against a broad spectrum of fish diseases.

12. Claims 22, 46 and 47 are rejected under 35 U.S.C. 103(a) unpatentable over Wolf-Watz et al, Fang et al, Wang et al as set forth above for claims 1-3, 5-6, 10-13,

15-16, 20-21, 27-36, 45 and 48 and further in view of Morinigo et al (*Bulletin of the European Association of Fish Pathologists*, Nov.2, 2002, Vol. 22, No.5, p. 298-303).

Claims 22 and 46-47 are drawn to the oral vaccine of claim 1 further comprising bacterial antigens of killed bacteria selected from the group consisting of bacterial antigens or killed bacteria selected from the group consisting of *Shewanella putrefaciens*, *Pseudomonas fluorescens*, *Vibrio alginolyticus* and *Flexibacter columnaris*.

Wolf-Watz et al and Wang et al as combined above do not teach *Vibrio alginolyticus*.

Morinigo et al teach that a divalent vaccine composition comprising *Vibrio alginolyticus* and *Photobacterium damsela* subsp. *Piscicida*. Morinigo et al teach that the concentration of protein 800 mg ml⁻¹ (page 299). Morinigo et al teach that high protection was conferred by the divalent vaccine (page (302)).

It would be *prima facie* obvious at the time the invention was made to add the *Vibrio alginolyticus* and *Photobacterium damsela* subsp. *Piscicida* antigens as taught by Morinigo et al to the vaccine composition of Wolf-Watz et al and Wang et al as combined above because Wolf-Watz et al teach that the vaccine of the invention may comprise one or more antigens that are pathogenic to fish to produce a vaccine that provides broad spectrum protection against a range of fish pathogens (column 7). It would be expected barring evidence to the contrary that a vaccine comprising proteins from *Aeromonas hydrophila*, immobilization antigen repeat I of *Ichthyophythrirus*; and *Vibrio alginolyticus* and *Photobacterium damsela* subsp. *Piscicida* antigens would be

Status of Claims

14. No claims allowed.


Conclusion

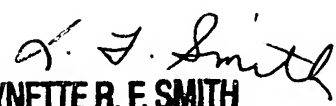
15. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov/>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


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April 12, 2006


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